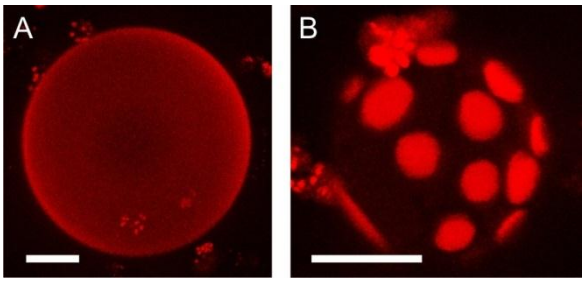
Project C3: Adhesion-induced domain formation in multicomponent membranes

Project leader: **Dimova (MPIKG)**
Co-supervisor: **Hildebrandt (TUB)**
US partner: **Discher (UPenn)**

Outline. In the last years, the outburst of studies on multicomponent model membranes has been gradually shaping our understanding about cell membranes. The emerging concept pictures them as heterogeneous patchworks of groups of lipids, cholesterol and integral proteins. Intramembrane domains or the so-called lipid rafts are thought to be involved in many biological processes. In model lipid systems, domain formation arises from the intramembrane interactions between the different membrane components. Phase separation can be directly visualized with fluorescence microscopy on giant vesicles as model systems (see figure). Another system, for which patterns of membrane domains may be observed are bilayer membranes adhering to rigid substrates. In this case, the domain formation is induced not only by the intramembrane molecular interactions but also by the interactions between the lipid molecules and the substrate.



Confocal 3d images of multicomponent giant unilamellar vesicles. (A) No phase separation is observed when the membrane composition belongs to the single fluid phase region of the phase diagram. (B) Fluid domains are formed in membranes with composition belonging to the two fluid phase coexistence region. Scale bars correspond to 10 μm.

Research within the German group. As a model membrane system we will employ giant unilamellar vesicles made of binary lipid mixtures or the ternary mixture dioleoylphosphatidylglycerol (a negatively charged lipid), egg sphingomyelin, and cholesterol. The phase diagram of the latter was recently reported and the region of coexistence of liquid ordered and liquid disordered phases located. As adhesive substrates we will employ either flat substrates coated with the positively charged protein cytochrome c and streptavidin-coated particles binding to biotinylated lipids in the membrane. Vesicles in the single fluid phase region but close to the phase coexistence boundary will be brought to the substrate and examined for domain formation using conventional fluorescence or confocal microscopy. The membrane bending rigidity and surface charge will be characterized using fluctuation analysis and zeta-potential measurements, respectively. The adhesion strength could be evaluated from the morphology of the adhering vesicle and will be modulated by changing the ionic strength of the bathing medium.

Longer-term perspective. In the continuation period we will employ manipulation of the particles (as adhesive substrate) with optical tweezers which would allow for control of the adhesion protocol. We also envision studying vesicle adhesion to glass substrates coated with a self-assembled monolayer of oligomers exposing a positive charge in the medium.

Complementary work in US partner group. The group of Discher studies the adhesion of cells to particles (endocytosis-related phenomena) and a variety of substrates that differ in their mechanical stiffness. During the stay with Discher, the doctoral researcher will explore membrane adhesion to substrates with variable functional groups and rigidity.

Status of the project. Experimental data will be compared to numerical results obtained in project C4 (Lipowsky) where domain formation in adhering membranes is studied using Monte Carlo and DPD codes. The work will be pursued also in close collaboration with project C2 (Hildebrandt), in which multicomponent membranes are studied experimentally and the effect of cytochrome c is investigated. Other closely related projects are B1 (Weikl) and B2 (Gradzielski), theoretically and experimentally exploring interactions between membranes and colloidal particles. The growth of patterns/domains in membranes is similar to processes in monolayers studied in project A4 (Riegler).